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Response under 37 C.F.R. 1.116

Appln. Ser. No.:	Filed:	Inventor(s):	Atty Dkt:
09/576,597	22 May 2000	J. Voorhees	100UM-009A
Title: Compositions and Methods for Use Against Acne-Induced Inflammation and Dermal Matrix-Degrading Enzymes			
Examiner: V. Kim			Art Unit: 1614

Asst. Comm'r for Patents
Washington, D.C. 20231-0001

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RESPONSE AFTER FINAL REJECTION

Dear Sir:

In complete and timely response to the office action mailed 5 December 2001, in which the rejections were designated as final, Applicants request reconsideration and reexamination of the subject application.

Amendments

Please first amend the application by cancelling claims 6 and 7.

Finality of Office Action

The examiner alleges that the previous amendments necessitated designating this rejection as final. As the previous amendments to claim 1 were narrowing amendments and merely incorporated the limitations of dependent claim 2 into claim 1, the amendments did not necessitate designating this rejection as final. Accordingly, the finality of the rejection should be withdrawn as premature (MPEP 706.07(a)and (d)). Further, there is no established point of contention between Applicants and the Office, as the claims were amended in light of the Oliver reference cited by the examiner.

Rejections under 35 U.S.C. 112[1] and 112[2]

The examiner alleges that the specification does not comply with the best mode requirement for claims 1, 3-9, and 21, which rejection is respectfully traversed because the rejection provides no reasoning that there is (or may be) any mode better than disclosed for differentiating non-antioxidant MMP inhibitors from antioxidant MMP inhibitors. The examiner will note that *every* compound described in the specification is an existing compound; there are no compounds claimed that are *per se* novel. Applicants' *in vivo* human experiments describe which compounds were used, and the background section of the application, replete with references, is based on literature searches rather than experiments.

The rejection also alleges it would take undue experimentation to know which MMP inhibitors are antioxidants, even through the term "antioxidant" is well-known and understood by those of ordinary skill. The rejection does not explain why any experimentation to determine whether a compound is an MMP inhibitor and/or is (is not) an antioxidant would be "undue". *In re Armbruster*, 185 U.S.P.Q. 152 (C.C.P.A. 1975). Applicants need not list, nor test, all possible compounds within the scope of the claim. Given the prevalence with which "anti-oxidant" compounds are described in present day literature, the rejection lacks any supporting reasoning that the claims are not enabled.

The rejection alleges that it is not clear whether anti-oxidant MMP inhibitors are excluded from the claims as now amended. The amendment specifies that the non-antioxidant inhibitor "is selected from the group consisting of . . . elastase inhibitors." Accordingly, if proanthocyanidine is described as an antioxidant and an elastase inhibitor, it clearly would be excluded from the claims. That one might have to do routine experimentation to determine whether a given compound is an antioxidant MMP inhibitor does not violate the second paragraph of § 112.

Because Applicants do not devise new molecules, they (like the examiner) must rely on conventional wisdom for determining which existing compounds are potential candidates for use in the present invention, and they must also test the compounds to determine whether they inhibit MMPs and/or oxidants.

Rejections under 35 U.S.C. 103

Claims 1-5 and 9 stand rejected hereunder as obvious over Zeligs, which rejection is respectfully traversed.

While Zeligs teaches DHEA can be used for skin conditions, "[t]he side effects [of DHEA administration] of increased sebum production and associated acne, caused by DHEA's stimulation of sebaceous gland tissue, are reduce by the drying effect of retinoids." (Col. 3, ln. 21-24; emphasis added.) In fact, the only mention of "acne" by Zeligs is as a side-effect of DHEA administration, so Zeligs does not suggest any treatment for acne, nor appreciate anything about acne scarring.

Acne is taught by Zeligs to be a side effect of the administration of DHEA. Accordingly, the reference teaches away from using DHEA to treat acne, and so these claims would not have been obvious from Zeligs. Contrary to the examiner's contention, if DHEA causes increased sebum production, one would not have been motivated to use it on acne skin because of the likelihood of exacerbating the condition. In fact, Zeligs uses DHEA because it increases sebum production (because it ameliorates excessive skin dryness, at col. 3, ln. 27). The present claims would not have been obvious over Zeligs.

Claims 8 and 21 stand rejected as obvious over Lanzendörfer, which rejection is respectfully traversed. In connection with the substance of this rejection, submitted is another declaration from Dr. Kang under 37 C.F.R. 1.132, in which he makes clear that Lanzendörfer does not appear to appreciate that all acne is not alike. For example, a dermatologist of ordinary skill would not treat cosmetic, chemical, or mechanical acne with any composition (as taught by Lanzendörfer), but would first eliminate the suspected source of the problem instead of putting a composition on already inflammed skin (¶4).

Still further, the examiner oversimplifies the limitiations of claim 8, which requires the combination of an MMP inhibitor and a neutrophil elastase inhibitor. That Applicants disclose "caffeic acid *derivatives*" as potential elastase inhibitors does not mean that all caffeic acid derivatives are elastase inhibitors. And since Lanzendörfer provides no teaching about enzymes that degrade collagen (hence the need for MMP inhibition) or elastin (hence the need for elastase inhibition), or that these occur in acne lesions, the invention of claim 8 or claim 21 would not

have been obvious from this reference. That it may be possible, given all the possible combinations of substances disclosed by Lanzendörfer, to make a composition that happens to have both an MMP inhibitor and a neutrophil elastase inhibit is the antithesis of obviousness: one is forced to make every possible combination because there is no teaching about what is required, or sufficient, for the claimed method.

So the examiner's suggestion to use "caffeic acid" does not provide to the patient any MMP or elastase inhibition, as not all caffeic acid derivatives are enzyme inhibitors. Cyclosporin-A is typically used as an immunomodulator, whereas Lanzendörfer states nothing more than that cyclosporin-A is a "conventional active system," which has no art-recognized meaning; all of those "conventional" system components disclosed by Lanzendörfer are immunomodulating compounds. So even combining "caffeic acid, cyclosporine A, and an antimicrobial agent" does not achieve the claimed combination of an antibacterial in combination with both an MMP inhibitor and an elastase inhibitor.

The statement in the rejection that the motivation to combine is not understood because each of the references is used singly, not in combination.

Conclusion

In light of the foregoing, withdrawal of the finality of the rejection, and withdrawal of the particular rejections, are now believed to be in order, and are earnestly solicited, and so allowance of the claim is believed next in order.

CERTIFICATE OF MAILING OR TRANSMISSION – 37 CFR 1.8

I hereby certify that I have a reasonable basis that this paper, along with any referred to above, (i) are being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D C 20231, or (ii) are being transmitted to the U.S. Patent & Trademark Office in accordance with 37 CFR § 1.6(d).

DATE: 5 March 2002

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Respectfully submitted,

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